REMARKS

By this Amendment, applicant is replacing existing claims 1, 6, 7, 9 and 10 with new claims 1, 6, 7, 9 and 10, above. Attached hereto as Appendix A is a marked-up version showing the changes made to the claims herein. Applicant retains the right to file one or more divisional or continuation patent applications claiming the deleted subject matter.

Applicant by this Amendment has amended the claims of the subject application so that they are restricted to compounds of Group I, which applicant elected without traverse in the Communication filed March 26, 2002. It is noted that the Examiner has maintained that the originally-claimed subject matter falling outside of the scope of Group I is drawn to subject matter that is patentably distinct from the subject matter of Group I.

Applicant asserts that the rejections recited in (1)(a) and (2) of the May 1, 2002 Office Action are rendered moot in light of the restriction herein of the claims to Group I.

Applicant has herein replaced the terms such as "comprises", "contain", "contains" and "containing" recited in claims 1, 6 and 7 with the terms "includes" and the like in order to overcome the rejection recited in (1)(b) of the May 1, 2002 Office Action.

The Examiner has asserted in (1)(c) of the May 1, 2002 Office Action that the term "carbocyclic ring" where used to include heterocyclic ring in the claims is repugnant to the "usual" meaning of the term "carbocyclic ring". In view thereof, applicant has deleted from the claims those recitations of "carbocyclic" which encompassed "heterocyclic".

The Examiner has also asserted in (1)(c) that the term "alkyl" as in "alkyl . . . optionally contain one double or triple bond" in the claims is repugnant to the "usual meaning of the term "alkyl". According to the Examiner, the accepted meaning is "saturated carbon chain" only.

Applicant respectfully traverses this rejection. Applicant maintains that the term "alkyl" can be recognized in the art to refer to hydrocarbon chains comprising one or more unsaturated bonds. As evidence thereof, applicant attaches hereto a copy of page 834of Organic Chemistry, Third Edition, T. W. Graham Solomons, University of South Florida, John Wiley & Sons, Inc. (1984), an organic chemistry textbook well accepted in the art. Solomons uses the term "alkyl" in "alkylamines", and uses "alkylamines" to refer not only to amines comprising saturated hydrocarbon moieties, such as ethylamine, but also to amines comprising unsaturated groups, such as allylamine. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw the rejection recited in

(1)(c) with respect to applicant's use of the term "alkyl".

Applicant has deleted the clause containing the word "preferably" in claims 6 and 7, in response to the Examiner's rejection recited in (1)(c).

Applicant has deleted the clause containing the phrase "including but not limited to" in claims 9 and 10 in view of (1)(d).

The Examiner rejected claim 12-16 and 18-22 under 35 USC 112, first paragraph, in (3). According to the Examiner, the specification provides no guidance for combination therapy. The Examiner stated that formulation of a combined therapy requires undue experimentation and even co-administration requires extensive research because drugs can allegedly interact with each other by inhibiting metabolism and protein binding.

Applicant respectfully traverses this rejection. The specification described formulation and administration methods on pages 30-31. Moreover, the Examiner has provided no concrete reasons or evidence that the compounds recited in applicant's claims would be contra-indicated by any other drug, generally or specifically.

The Examiner rejected claims 1, 6, 7, 9-11 and 17 under the judicially created doctrine of obviousness-type double patenting as allegedly obvious over the claims of US Patent No. 5,962,479 (hereinafter '479). It is noted that the Examiner did not reject claims 2-5, 8, 12-16 and 18-22 as obvious over the claims of '479. Applicant will consider filing a terminal disclaimer upon consideration of otherwise allowable subject matter.

Claim 8 should no longer be objected to, since the claim from which it depends should now be deemed allowable by the Examiner.

It is believed that the amendments herein overcome the Examiner's rejections and objections set forth in the May 1, 2002 Office Action. Applicant hereby requests the earliest possible notification of allowable subject matter.

If a Telephone Interview would be of assistance in advancing the prosecution of this application, the Examiner is kindly to telephone Applicant's' undersigned attorney at the telephone provided.

No fee, other then the fee for the three month extension of time authorized in the Petition filed herewith is believe necessary for filing this Amendment. However, if any other fee is found necessary for filing this Amendment, authorization to charge such fee to Deposit Account No. 16-1445 is hereby given.

Respectfully submitted,

Date: November 1, 2002

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THIRD EDITION

T. W. Graham Solomons
University of South Florida

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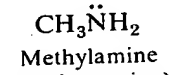
19

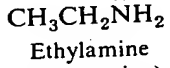
Amines

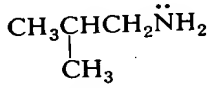
19.1 NOMENCLATURE

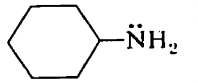
In common nomenclature most primary amines are named as *alkylamines*. In systematic nomenclature (in parentheses below) they are named by adding the suffix *-amine* to the name of the chain or ring system to which the NH_2 group is attached with elision of the final *e*.

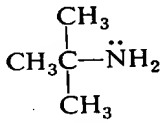
Primary Amines

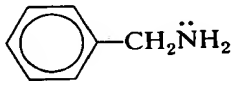

Methylamine
(Methanamine)


Ethylamine
(Ethanamine)


Isobutylamine
(2-Methyl-1-propan-
amine)


Cyclohexylamine
(Cyclohexanamine)

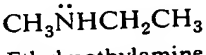

tert-Butylamine
(2-Methyl-2-propanamine)

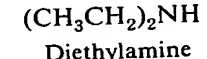

Benzylamine
(Phenylmethanamine)


Allylamine
(2-Propenamine)

Most secondary and tertiary amines are named in the same general way. In common nomenclature we either designate the organic groups individually if they are different, or use the prefixes *di-* or *tri-* if they are the same. In systematic nomenclature we use the locant *N* to designate substituents attached to nitrogen.

Secondary Amines


Ethylmethylamine
(*N*-Methylethanamine)

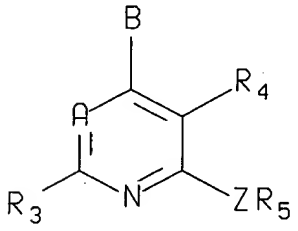

Diethylamine
(*N*-Ethylethanamine)

APPENDIX A

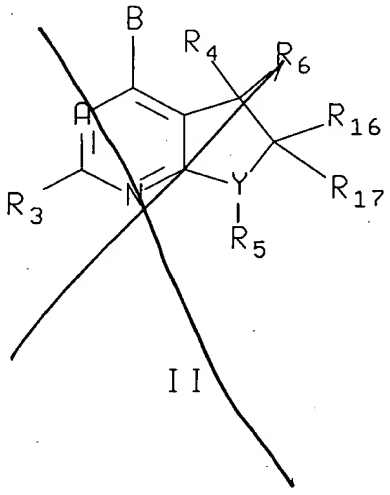
Claims 1, 6, 7, 9 and 10 are amended as follows:

VERSION WITH MARKINGS TO SHOW CHANGES MADE – DO NOT ENTER:

1. (Amended) A compound of the formula

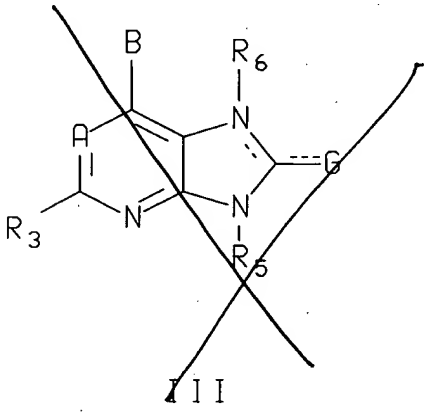


I



II

~~or~~



III

or a pharmaceutically acceptable salt thereof, wherein

~~[the dashed lines represent optional double bonds, with the proviso that when the dashed line in C—G represent a double bond, then the dashed line in N(R_6)—C does not represent a double~~

~~bond; and with the proviso that when the dashed line in $N(R_6)$—C represents a double bond, R_6 is absent in formula III and the dashed line in C—G does not represent a double bond;~~]

A is $-CR_7$ [~~or N~~];

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_1$, $-CHR_1OR_2$, $-CHR_2SR_1$, $-C(S)R_2$, $-C(O)R_2$, $-CHR_2NR_1R_2$, $-CHR_1NHR_2$, $-CHR_1N(CH_3)R_2$, or $-NR_{12}NR_1R_2$;

[~~when the dashed line in C—G represents a double bond, then G is hydrogen, oxygen, sulfur, NH, or $N(C_1$-C_4 alkyl);~~

~~when the dashed line in C—G does not represent a double bond, then C—G is C(H)(NH_2), CH_2, C(H)(methoxy), C(H)(ethoxy), C(H)(O(C_2-C_4 alkyl)), C(H)(halo), C(H)(trifluoromethoxy), C(H)(methyl), C(H)(ethyl), C(H)(C_3-C_4 alkyl), C(H)(S(C_1-C_4 alkyl)), C(C_1-C_4 alkyl)(C_1-C_4 alkyl), cyclopropyl, C(H)(cyclopropyl), thiomethoxy, C(H)(NH_2), C(H)($NHCH_3$), C(H)($N(CH_3)_2$), or C(H)(trifluoromethyl);~~

~~wherein said cyclopropyl, methoxy, ethoxy, C_2-C_4 alkyl, and C_1-C_4 alkyl groups of C—G may optionally be substituted by one OH, methoxy, or trifluoromethoxy, or may optionally be substituted by from one to six fluoro atoms;~~

~~Y is CH or N;~~]

Z is NH, O, S, $-N(C_1$-C_2 alkyl), $-NC(O)CF_3$, or $-C(R_{13}R_{14})$, wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-C(R_{13}R_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5, which ring optionally [~~comprises~~] includes two or three further hetero members selected independently from oxygen, nitrogen, NR_{12}, and $S(O)_m$, and optionally [~~comprises~~] includes from one to three double bonds, and is optionally substituted with halo, C_1-C_4 alkyl, $-O(C_1$-C_4 alkyl), NH_2, $NHCH_3$, $N(CH_3)_2$, CF_3, or OCF_3, with the proviso that said ring does not [~~contain~~] include any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and does not [~~comprise~~] include more than two oxygen or $S(O)_m$ heterologous members;

R_1 is C(O)H, $C(O)(C_1$-C_6 alkyl), $C(O)(C_1$-C_6 alkylene)(C_3-C_8 cycloalkyl), $C(O)(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), $C(O)(C_1$-C_6 alkylene)(C_4-C_8 heterocycloalkyl), $-C(O)(C_3$-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, $-(C_1$-C_6 alkylene)(C_3-C_8 cycloalkyl), $-(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), $-(C_1$-C_6 alkylene)(C_4-C_8 heterocycloalkyl), $-(C_3$-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), or –O-aryl, or $–O-(C_1$-C_6 alkylene)-aryl; wherein said aryl, C_4-C_8 heterocycloalkyl, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_3-C_8

cycloalkylene, and C_1-C_5 alkylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 alkyl, -C_3-C_8 cycloalkyl, hydroxy, chioro, bromo, iodo, CF_3, -O-(C_1-C_6 alkyl), -O-(C_3-C_5 cycloalkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(R_{24})(R_{25}), -N(R_{24})(R_{25}), -S(C_1-C_4 alkyl), -S(C_3-C_5 cycloalkyl), -N(C_1-C_4alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl), -COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I^-, -SO(C_1-C_4 alkyl) and -SO_2(C_1-C_4 alkyl); and wherein the C_1-C_6 alkyl, C_1-C_6 alkylene, C_5-C_8 cycloalkyl, C_5-C_8 cycloalkylene, and C_5-C_8 heterocycloalkyl moieties of R_1 may optionally independently [~~contain~~] include from one to three double or triple bonds; and wherein the C_1-C_4 alkyl moieties and C_1-C_6 alkyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, -CH_2-aryl, C_3-C_5 cycloalkyl, or –O-(C_1-C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally [~~contain~~] include one or two double or triple bonds; and wherein each heterocycloalkyl group of R_1 [~~contains~~] includes from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

R_2 is hydrogen, C_1-C_{12} alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_1-C_6 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, –(C_1-C_6 alkylene)aryl, or -(C_3-C_8 cycloalkylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, -OH, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_6 alkyl), -S(O)(C_1-C_6 alkyl), -$S(O)_2$(C_1-C_6 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I^-, CN, and NO_2; and wherein the C_1-C_{12} alkyl, -(C_1-C_6 alkylene), -(C_5-C_8 cycloalkyl), -(C_5-C_8 cycloalkylene), and -(C_5-C_8 heterocycloalkyl) moieties of R_2 may optionally independently [~~contain~~] include from one to three double or triple bonds; and wherein each heterocycloalkyl group of R_2 [~~contains~~] includes from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

or when R_1 and R_2 are as in –NHCHR_1R_2, -OCHR_1R_2, -SCHR_1R_2, –CHR_1R_2 or -NR_1R_2, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally [~~contain~~] include one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12}; and which [~~carbocyclic~~] ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1-C_4 alkyl, fluoro, chloro,

bromo, iodo, CF_3, -O-(C_1-C_4 alkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -S(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl),-COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), and $-SO_2$(C_1-C_4 alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, NH_2, NH(C_1-C_2 alkyl), $N(CH_3)_2$, -$NHCOCF_3$, -$NHCH_2CF_3$, $S(O)_m$(C_1-C_4 alkyl), $CONH_2$, -$CONHCH_3$, $CON(CH_3)_2$, -CF_3, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 alkyl, C_3-C_5 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR_{24}, C_1-C_6 alkoxy, -O-(C_3-C_5 cycloalkyl), -O-(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), -$CH_2SC(S)O$(C_1-C_4 alkyl), -CH_2OCF_3, CF_3, amino, nitro, -$NR_{24}R_{25}$, -(C_1-C_4 alkylene)-OR_{24}, -(C_1-C_4 alkylene)Cl, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, -$NHCOR_{24}$, -$NHCONR_{24}R_{25}$, -C=NOR_{24}, -$NHNR_{24}R_{25}$, -$S(O)_mR_{24}$, -$C(O)R_{24}$, -$OC(O)R_{24}$, -C(O)CN, -$C(O)NR_{24}R_{25}$, -$C(O)NHNR_{24}R_{25}$, and $-COOR_{24}$, wherein the alkyl and alkylene groups of R_4 may optionally independently ~~[contain]~~ include one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, -$NHCOCH_3$, -$NHCOCH_2Cl$, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)(C_1-C_2 alkyl), -COO(C_1-C_4 alkyl), -COOH, -CO(C_1-C_4 alkyl), C_1-C_6 alkoxy, C_1-C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1-C_{10} alkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_1-C_4 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkyl), -(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, nitro, cyano, -$NR_{24}R_{25}$, -$NR_{24}COR_{25}$, -$NR_{24}CO_2R_{26}$, -COR_{24}, -OR_{25}, -$CONR_{24}R_{25}$, -$CO(NOR_{22})R_{23}$, -CO_2R_{26}, -C=$N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1-C_{10} alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkylene), (C_3-C_8 cycloalkyl), (C_3-C_8 cycloalkylene), and (C_4-C_8 heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected form C_1-C_4 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, hydroxy, C_1-C_6 alkoxy, nitro halo, cyano, -$NR_{24}R_{25}$, -$NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, -COR_{24}, -OR_{25}, -$CONR_{24}R_{25}$, CO_2R_{26}, -$CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7

membered ring, saturated or unsaturated, fused to R^5, which ring optionally can [~~contain~~] include one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any –S-S-, -O-O-, -S-O-, or –N-S- bonds, and which ring is optionally substituted with C_1-C_4 alkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cyloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, nitro, halo, cyano $–NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{26})R_{25}$, or $–S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27} can further be selected from -SO_2NH(C_1-C_4 alkyl), -SO_2NH(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -SO_2NH(C_3-C_8 cycloalkyl), -SO_2NH(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -SO_2N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -SO_2NH_2, -$NHSO_2$(C_1-C_4 alkyl), -$NHSO_2$(C_3-C_8 cycloalkyl), -$NHSO_2$(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), and -$NHSO_2$(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl); and wherein the alkyl, and alkylene groups of R_5 may independently optionally [~~contain~~] include one double or triple bond;

R_6 is hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), or –(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

[or, wherein the compound is a compound of formula II, R_6 and R_4 can together form an oxo (=O) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO_m, N, and NR_{12}, but not containing any -O-O-, -S-O-, -S-S-, or –N-S- bonds, and further optionally substituted with C_1-C_4 alkyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 alkyl substituent may optionally contain one double or triple bond;]

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C_1-C_2 alkyl), -O(cyclopropyl), -COO(C_1-C_2 alkyl), -COO(C_3-C_8 cycloalkyl), $-OCF_3$, CF_3, $-CH_2OH$, or CH_2OCH_3;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl;

~~[R_{16} and R_{17} are each, independently, hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that R_{16} and R_{17} are not both methoxy or ethoxy;~~

~~or R_{16} and R_{17} together form an oxo (=O) group;~~

~~or R_{16} and R_{17} are connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing from one to three heterologous ring members selected from O, SO_m, N, and NR_{12}, but not containing any -O-O-, -S-O-, -S-S-, or –N-S-~~

~~bonds, and further optionally substituted with C_1-C_4 alkyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 alkyl substituent may optionally contain one double or triple bond;~~]

R_{22} is independently at each occurrence selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4 alkylene)(C_3-C_8 cycloalkyl);

R_{23} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_2-C_8 alkoxyalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, -(C_1-C_4 alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R_{24} and R_{25} are independently at each occurrence selected from hydrogen, -C_1-C_4 alkyl, C_1-C_4 haloalkyl, especially CF_3, -CHF_2, CF_2CF_3, or CH_2CF_3, -(C_1-C_4 alkylene)OH, -(C_1-C_4 alkylene)-O-(C_1-C_4 alkyl), -(C_1-C_4 alkylene)-O-(C_3-C_5 cycloalkyl), C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -C_4-C_8 heterocycloalkyl, -(C_1-C_4 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl), wherein the -C_4-C_8 heterocycloalkyl groups can each independently optionally be substituted with aryl, CH_2-aryl, or C_1-C_4 alkyl, and can optionally [~~contain~~] include one or two double or triple bonds; or, when R_{24} and R_{25} are as $NR_{24}R_{25}$, -$C(O)NR_{24}R_{25}$, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, or -$NHCONR_{24}R_{25}$, then $NR_{24}R_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally [~~containing~~] including one or two further hetero members independently selected from $S(O)_m$, oxygen, nitrogen, and NR_{12}, and optionally [~~containing~~] including from one to three double bonds;

R_{26} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocycloalkyl groups of the compound of formula I, II, or III do not [~~comprise~~] include any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and do not [~~comprise~~] include more than two oxygen or $S(O)_m$ heterologous members.

6. (Amended) A compound of formula I according to claim 1, wherein Z is O; B is –$NHCHR_1R_2$, wherein R_1 is -C(O)H, -C(O)(C_1-C_6 alkyl), or –C_1-C_6 alkyl, wherein said C_1-C_6 alkyl is optionally substituted with from one to six fluoro atoms or one or two R_8 independently selected from –C_1-C_4 alkyl, hydroxy and –O-(C_1-C_6 alkyl), and wherein R_2 is –C_1-C_{12} alkyl

optionally [~~containing~~] including from one to three double or triple bonds and optionally substituted with from one three substituents selected from fluoro and C_1-C_6 alkyl; R_5 is phenyl, pyridyl or pyrimidyl, substituted with two or three R_{27} groups selected from halo, -(C_1-C_4 haloalkyl), -$C(O)R_{24}$, -OR_{25}, -$C(O)NR_{24}R_{25}$, and C_1-C_{10} alkyl which is optionally substituted with one to three substituents[~~, preferably one substituent,~~] selected from hydroxy, C_1-C_6 alkoxy, and –$NR_{24}R_{25}$; and R_4 is -$C(O)NR_{24}R_{25}$.

7. (Amended) A compound of formula I according to claim 1, wherein Z is O; B is -$NHCHR_1R_2$, wherein R_1 of –$NHCHR_1R_2$ is -C(O)H, -C(O)(C_1-C_6 alkyl), or –C_1-C_6 alkyl, wherein said C_1-C_6 alkyl is optionally substituted with from one to six fluoro atoms or one or two R_8 independently selected from –C_1-C_4 alkyl, hydroxy and –O-(C_1-C_6 alkyl), and wherein R_2 of –$NHCHR_1R_2$ is –C_1-C_{12} alkyl optionally [~~containing~~] including from one to three double or triple bonds and optionally substituted with from one three substituents selected from fluoro and C_1-C_6 alkyl; R_5 is phenyl, pyridyl or pyrimidyl, substituted with two or three R_{27} groups selected from halo, -(C_1-C_4 haloalkyl), -$C(O)R_{24}$, -OR_{25}, -$C(O)NR_{24}R_{25}$, and C_1-C_{10} alkyl which is optionally substituted with one to three substituents[~~, preferably one substituent,~~] selected from hydroxy, C_1-C_6 alkoxy, and –$NR_{24}R_{25}$; and R_4 is –NR_1R_2, wherein R_1 of –NR_1R_2 is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, or -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), and R_2 of –NR_1R_2 is C_1-C_{12} alkyl optionally [~~containing~~] including from one to three double or triple bonds and optionally substituted with from one three fluoro atoms.

9. A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF[~~, including but not limited to disorders induced or facilitated by CRF~~], or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease;

gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma, spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

10. A method for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF[~~, including but not limited to disorders induced or facilitated by CRF~~], or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer, diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage,

including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder or condition.